

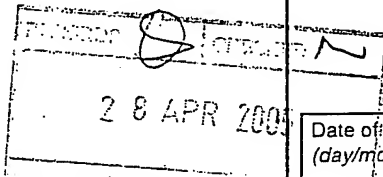
PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

To:
ERIC POTTER CLARKSON
Attn. Pilkington, Stephanie
Park View House
58 The Ropewalk
Nottingham NG1 5DD
UNITED KINGDOM

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT AND
THE WRITTEN OPINION OF THE INTERNATIONAL
SEARCHING AUTHORITY, OR THE DECLARATION



(PCT Rule 44.1)

Date of mailing
(day/month/year) 28/04/2005

Applicant's or agent's file reference

DUNY/P30950PC

FOR FURTHER ACTION See paragraphs 1 and 4 below

International application No.

PCT/GB2004/003096

International filing date

(day/month/year) 16/07/2004

Applicant

UNIVERSITY OF DUNDEE

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.
3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Reminders

Shortly after the expiration of 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within 19 months from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later); otherwise, the applicant must, within 20 months from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of 30 months (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
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Authorized officer

Geertruida Groeneveld-Van der Spek

(See notes on accompanying sheet)

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the *PCT Applicant's Guide*, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report and the written opinion of the International Searching Authority, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only (see *PCT Applicant's Guide*, Annexes B1 and B2).

The attention of the applicant is drawn to the fact that amendments to the claims under Article 19 are not allowed where the International Searching Authority has declared, under Article 17(2), that no international search report would be established (see *PCT Applicant's Guide*, Volume I/A, paragraph 296).

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference DUNY/P30950PC	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/GB2004/003096	International filing date (day/month/year) 16/07/2004	(Earliest) Priority Date (day/month/year) 17/07/2003
Applicant UNIVERSITY OF DUNDEE		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 9 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. ☒ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.

2. ☐ Certain claims were found unsearchable (See Box II).

3. ☐ Unity of invention is lacking (see Box III).

4. With regard to the title,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

METHODS FOR USE OF AN LKB1/STRAD7MO25 COMPLEX

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the drawings,

- a. the figure of the drawings to be published with the abstract is Figure No. 21b

☒ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

- b. ☐ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/GB2004/003096

Box No. 1 Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
 - a. type of material
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing
 - ☐ contained in the international application as filed
 - ☐ filed together with the international application in computer readable form
 - ☒ furnished subsequently to this Authority for the purpose of search
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K14/82 C12N9/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HAWLEY S A ET AL: "Characterization of the AMP-activated protein kinase kinase from rat liver and identification of threonine 172 as the major site at which it phosphorylates AMP-activated protein kinase." THE JOURNAL OF BIOLOGICAL CHEMISTRY. 1 NOV 1996, vol. 271, no. 44, 1 November 1996 (1996-11-01), pages 27879-27887, XP002315194 ISSN: 0021-9258 the whole document ----- -/--	1-7, 11-19, 22,23, 30,32, 33,37-39

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

28 January 2005

Date of mailing of the international search report

28. 04. 2005

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Smalt, R

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE WPI Section Ch, Week 200222 Derwent Publications Ltd., London, GB; Class B04, AN 2002-171818 XP002315199 & WO 02/06520 A1 (CHUGAI RES INST MOLECULAR MEDICINE INC) 24 January 2002 (2002-01-24) the whole document -& WO 02/06520 A1 (CHUGAI RES INST MOLECULAR MEDICINE INC) 24 January 2002 (2002-01-24)</p>	1
X	<p>BAAS A F ET AL: "Activation of the tumour suppressor kinase LKB1 by the STE20-like pseudokinase STRAD" EMBO JOURNAL, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 22, no. 12, 16 June 2003 (2003-06-16), pages 3062-3072, XP002298130 ISSN: 0261-4189 the whole document</p>	28,29
A	<p>BOUDEAU J ET AL: "LKB1, a protein kinase regulating cell proliferation and polarity" FEBS LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 546, no. 1, 3 July 2003 (2003-07-03), pages 159-165, XP004433636 ISSN: 0014-5793 the whole document</p>	
A	<p>NATH NANDITA ET AL: "Yeast Pak1 kinase associates with and activates Snf1." MOLECULAR AND CELLULAR BIOLOGY. JUN 2003, vol. 23, no. 11, June 2003 (2003-06), pages 3909-3917, XP002315195 ISSN: 0270-7306 the whole document</p>	
A	<p>BEAULOYE^A^ ^B C ET AL: "Insulin antagonizes AMP-activated protein kinase activation by ischemia or anoxia in rat hearts, without affecting total adenine nucleotides" FEBS LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 505, no. 3, 21 September 2001 (2001-09-21), pages 348-352, XP004309604 ISSN: 0014-5793 the whole document</p>	

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	HAWLEY SIMON A ET AL: "Complexes between the LKB1 tumor suppressor, STRAD alpha/beta and M025 alpha/beta are upstream kinases in the AMP-activated protein kinase cascade." JOURNAL OF BIOLOGY (ONLINE) 2003, vol. 2, no. 4, 24 September 2003 (2003-09-24), page 28, XP002298131 ISSN: 1475-4924 the whole document	1,4-6, 15-23, 28-30, 32,33, 37-39
P,X	SHAW R J ET AL: "The tumor suppressor LKB1 kinase directly activates AMP-activated kinase and regulates apoptosis in response to energy stress" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 101, no. 10, 9 March 2004 (2004-03-09), pages 3329-3335, XP002298134 ISSN: 0027-8424 the whole document	1,24,25, 28-30, 32,33, 37-39
E	WO 2004/113562 A1 (MEDICAL RES COUNCIL [GB]; UNIV COLUMBIA [US]; CARLING DAVID [GB]; WOOD) 29 December 2004 (2004-12-29) the whole document	1-3,7,9, 11,12, 14-16, 18,20, 21,23, 32,33
T	BOUDEAU JÉRÔME ET AL: "M025alpha/beta interact with STRADalpha/beta enhancing their ability to bind, activate and localize LKB1 in the cytoplasm." THE EMBO JOURNAL. 1 OCT 2003, vol. 22, no. 19, 1 October 2003 (2003-10-01), pages 5102-5114, XP002315196 ISSN: 0261-4189 the whole document	
T	HONG SEUNG-PYO ET AL: "Activation of yeast Snf1 and mammalian AMP-activated protein kinase by upstream kinases." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA. 22 JUL 2003, vol. 100, no. 15, 22 July 2003 (2003-07-22), pages 8839-8843, XP002315197 ISSN: 0027-8424 the whole document	

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
T	<p>SUTHERLAND CATHERINE M ET AL: "Elm1p is one of three upstream kinases for the Saccharomyces cerevisiae SNF1 complex." CURRENT BIOLOGY : CB. 5 AUG 2003, vol. 13, no. 15, 5 August 2003 (2003-08-05), pages 1299-1305, XP002315198 ISSN: 0960-9822 the whole document</p>	
T	<p>WOODS A ET AL: "LKB1 is the upstream kinase in the AMP-activated protein kinase cascade" CURRENT BIOLOGY, CURRENT SCIENCE,, GB, vol. 13, no. 22, 11 November 2003 (2003-11-11), pages 2004-2008, XP002298132 ISSN: 0960-9822 the whole document</p>	
T	<p>LIZCANO J M ET AL: "LKB1 is a master kinase that activates 13 kinases of the AMPK subfamily, including MARK/PAR-1" EMBO JOURNAL, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 23, no. 4, 25 February 2004 (2004-02-25), pages 833-843, XP002298133 ISSN: 0261-4189 the whole document</p>	
T	<p>HARDIE D.G: "THE AMP-ACTIVATED PROTEIN KINASE PATHWAY - NEW PLAYERS UPSTEAM AND DOWNSTREAM" JOURNAL OF CELL SCIENCE, CAMBRIDGE UNIVERSITY PRESS, LONDON, GB, vol. 117, no. PART 23, 2004, pages 5479-5487, XP008040901 ISSN: 0021-9533 the whole document</p>	

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB2004/003096

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0206520	A1	24-01-2002	AU 7106701 A	30-01-2002
WO 2004113562	A1	29-12-2004	GB 2402938 A	22-12-2004
			US 2005026233 A1	03-02-2005

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB2004/003096

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-25,28-30,37-39 completely, and claims 32 and 33 partially

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-25,28-30,37-39 completely, and claims 32 and 33 partially

1.1. claims: 1-25,30 completely, and claims 31-32 partially

An LKB1 complex comprising STRAD and M025, preparation thereof, and its use in the identification of modulators of its phosphorylation of AMPK.

1.2. claims: 28,29

Method for identifying patients with PJS or an increased susceptibility thereto by analysing the STRAD and/or M025 genes for mutations.

1.3. claims: 37-39

AMPK subfamily members with a mutation replacing Thr172 and nucleic acids encoding them

2. claims: 26,27

Method for identifying binding partners of M025.

3. claims: 31 completely, and claims 32 and 33 partially

Use of an AMPK subfamily member in the manufacture of a medicament for treating diabetes or obesity.

4. claims: 34-36

Peptide substrates for LKB1 and antibodies reactive therewith
